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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,333	09/29/2005	Kenji Motokawa	082368-002100US	2713

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,333	MOTOKAWA ET AL.	
	Examiner	Art Unit	
	BAO LI	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,11 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,11 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/14/10&5/18/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

The response submitted on May 14, 2010 has been noted.

Status of claims:

Claims 1, 3, 5, 11 and 13 are pending and considered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1 and 5 are still rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

3. Applicants traverse the rejection and submit the following arguments:

a. The specification does not teach using type I FIPV N protein to induce neutralizing antibody. The induction of a neutralizing antibody is not the immune response related to a protective cellular immune response as claims drafted;

b. The claim 1 does not read on an astronomical number of variants. The variants with 1-5 amino acid mutations among the total 377 amino acids in length of polypeptide SEQ ID NO: 2 are just polypeptides having 96.1% identity to SEQ ID NO: 2, which are generally considered allowable give the function of the polypeptide is known. A person skill in the art is able to identify or isolate a polypeptide with a known immunogenic function.

c. The current claims have same issue as example 13 of 2008 written description guideline, such that antibodies can be generated when an antigen and antibody binding function is well known in the art. Because function of the claimed polypeptide of SEQ ID NO: 2 are immunogenic, one of skill in the art will readily recognize an immunogenicity

of a particular polypeptide, which rarely requires entire, residue-by residue sequence to remain unchanged, and the immunogenic activity is generally retained despite minor modification.

4. Applicants' argument has been respectfully considered; however, it is not found percussive for the reasons below:

5. 1). As Applicants admitted in the response, the immunological activity for the claimed polypeptide is only drawn to a regular antigenic property binding to an antibody, it is the one capable of inducing a protective T cell immune response. Therefore, the asserted antibody binding to an antigen is not applicable to the rejected claims;

6. 2). The specification in the instant Application has not identified and/or describes any immunogenic region or domain or T cell epitope responsible for the claimed protective T cell immune response. It is well known in the art that a T cell epitope is only about 10 to 20 amino acids long, sometime, it is about 5 to 9 amino acids long. As Applicants claims are directed to a genus of polypeptide comprising astronomic number of species, without a description about which structural/functional domain is responsible for the claimed function, a person skill in the art cannot visualize what kind of the mutant can be made for obtaining some broadly claimed variants of N protein SEQ ID NO: 2. Therefore, testing astronomic numbers of claimed polypeptide variants as claimed drafted with unexpected success is an undue experimentation.

7. 3) Especially, it is unpredictable using a N protein of FIPV to induce a protective immune response. Applicants also acknowledged that the field for developing IFPV vaccine is highly unpredictable. For example, a same N protein taught by Wasmoeon et al capable of inducing a protective immune response fail to produce any protective immune response by Vennema et al. Another expertise, Susan Little still commented in 2010 that the theory using a cellular immune response to protect Feline Infectious Peritonitis infection has not been established in the art (Susan Little, Feline Infectious Peritonitis published on line in the website of WINIE FELINE FOUNDATION 2010, page 1-6). Therefore, the assertion that one of skill in the art will readily recognize an immunogenicity of a particular polypeptide claimed protective immune response is supported by the current state of art. The argument is factual in view of the state of art.

8. 4). The claimed subject matter is directed to a genus of an antigenic polypeptide with astronomic number of variants as claims drafted. But, there is only one original polypeptide of N

protein set forth in SEQ ID NO: 2 is disclosed and tested for having the claimed protective immune response. No any other species has been described. No reduction of practice had been made. Therefore, a person skill in the art would not recognize that Applicants have the possession as the rejection claims broadly encompassed.

9. 5). In contract to Applicants' assertion, example 13 of 2008 written description does not have same issue as the one for the current claims. The example 13 in the 2008 written description guideline explains if an immunogenic polypeptide structure is known, making an antibody to said antigenic polypeptide/protein is a regular skill in the art. However, the current claims are directed to a genus of a polypeptide, which is more like the issue of examples 14 and 15, in which a claim directed to the species of antibody or species of polypeptide would satisfy the written description requirement, whereas the claimed a genus of an antibody or genus of polypeptide does not, if only a species of a polypeptide/protein is disclosed, and no structure and function as well as relationship between the structure and function for the genus of polypeptides have been fully described.

10. 6). Finally, Applicants are reminded that the enablement issue is a separate issue from a written description both under 371 USC 112 1st paragraph. MPEP § 2163.02 cites: "[a] n objective standard for determining compliance with the written description requirement is "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided that the purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Especially, the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. Because factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; absent a detail description of representative numbers of the claimed genus of polypeptide of SEQ ID NO: 2 variants, the skilled artisan could

not immediately recognize or distinguish members of the claimed genus of polypeptide variants. The full breadth of the claims does not meet the written description and enablement provision of 35 U.S.C. 112, first paragraph. The rejection is maintained.

11. Therefore, absence a representative number of species for the claimed genus of polypeptides, claims 1 and 5 fail to satisfy the written description requirement under 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The rejection of claims 1 and 3 under 35 U.S.C. 103(a) as being unpatentable over Wasmoen et al. (A) (US Patent 5,770,211) in view of Motokawa et al. (Microbiology and Immunology, 1996, Vol. 40, No. 6, pages 425-433) and Duphar International Research (EP 0 411 684 A2, 1991) and further substantiated by Wasmoen et al. (B) (Adv. Exp. Biol. 1995, Vol. 380, pp. 221-228) are maintained.

14. In the response, Applicants submit the following arguments to traverse the rejection:

15. 1). Even post filing date, the state of art teaches using N protein of FIPV as a vaccine composition is unpredictable, especially the FIPV can induce a humoral immune response that can exacerbate the infection due to an antibody dependent enhancement (ADE) effect as German et al. which is published after Wasmoen et al. There is no expectation of success.

16. 2). More suppressing result is that vaccine designed from type I N protein of FIPV conferred protection from challenge with type II FIPV,

17. 3). The disclosure taught by Wasmeon et al. is different from the one cited in claims in that i). Wasmeon et al. teach using the N protein from type II FIPV, ii).it is DNA vaccine rather than polypeptide vaccine; and iii) they use different virus to sensitize the animal prior to administration of N protein of FIPV. In contrast, the disclosed result shows that the claimed vaccine is sufficient for effectively protection.

18. 4). It is unpredictable that using an N protein of IFPV can induce a protective T cell immune response against type II FIPV rather then type I FIPV. For example, a DNA vaccine made by N protein of IFPV type I delivered by vaccinia virus cannot produce any protective immune response. Therefore, using the polypeptide with N protein from IFPV type I that has different structure than the one of type II IFPV is an unexpected result (Vennema et al. Virology 1991, Vol. 181, pp. 327-335).

19. Applicants' argument has been respectfully considered; it is found persuasive. First of all, the interpretation of the claimed subject matter does not consider the patentable weight for any preamble language cited in the claims. The only limitations are considered at the structural ingredient in the composition and active step f the method cited in claims. Moreover, the rejection is based on one of the claimed embodiments read on the N protein set forth in SEQ ID NO: 2 rather then any other variants.

20. To this context, because prior to the current Application was filed, the polypeptide N from type I FIPV had been completely disclose, and the method for using a N protein as an immunogenic polypeptide to stimulate an immune response had been taught, it would have been obvious for using the N protein of type II FIPV in combination with an adjuvant to make an immunogenic composition without any unexpected result for any ordinarily skill in the art. To this context, the rejection is maintained.

Claim Rejections - 35 USC § 112

21. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

22. The rejection of claims 1, 3, 5, 11 and 13 under 35 U.S.C. 112, first paragraph are moot in new of a new ground of rejection set forth below:

23. Claims 1, 3, 5, 11 and 13 are also rejected under 35 U.S.C. 112, first paragraph in this office action, because the specification, while being enabling for administering cats an immunogenic composition and a method for using it for inducing an immune response against type II FIPV infection, wherein the composition comprises the N protein set forth in SEQ ID

NO: 2, and an adjuvant composition comprising L80, aluminum hydroxide and **Feline inactivated trivalent vaccine** comprising feline herpes virus vaccine, an inactivated calicivirus and Chlamydia with boost immunizations for additional two times, does not reasonably provide enablement for having a vaccine and a method to protect cats from any IFVP infection **with any variants of a polypeptide** as claims drafted and also **with any vaccine adjuvant.** The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

24. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art with undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is one or more following factors in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988):

25. 1). Nature of invention, 2). Scope of claim encompassed, 3). State of art and Unpredictability of the field at the time of invention was filed, 4). Working example taught by the specification; 5).Guidance provided by the specification, 6). Level of skill in the art, and 7). Amount of work need to fulfill the scope of claims encompassed.

26. Upon further reviewing the disclosure of the current application, it is noted that the nature of invention is directed to an immunogenic composition comprising the N protein from type II IFPV set forth in SEQ ID NO: 2 and adjuvant composition comprising **Feline inactivated trivalent vaccine** Felidovac PRC (feline herpes virus vaccine, an inactivated calicivirus and Chlamydia) L80 and aluminum hydroxide to induce a protective immune response for FIPV type I after repeated three times of immunizations in cats.

27. However, the broad scope of claims read on a vaccine composition comprising any variants of FIPV II N protein set froth in SEQ ID NO: 2 and any adjuvant, wherein the composition is claimed to be able to induce a protective immune response against any FIPV infection.

28. The art for producing a universal vaccine for all genotypes of FIPV is unpredictable, because a protective immune response induced by the RNA virus of FIPV is very unstable and unpredictable as evidenced by Applicants' own work and other expertise's observation. In the

specification, Applicants teaches that said immunogenic composition is unexpectedly found to be able to induce more then 75% protective immune response for the FIPV type I infection in tested cats, but it is undetermined if said composition is able to induce a protective immuresponse to type I FIPV.

29. The state of art teaches that while the spike protein (S) of FIPV can induce a neutralizing antibody, but it does produce an antibody dependent enhancement of infection (ADE) rather then suppress the infection. The N protein from FIPV type II has been used for inducing a protective T cell mediated immune response delivered by a recombinant raccoon poxvirus vector. Applicants also assert the unpredictability for using a N protein to induce a protective immune response. For example, Applicants fail to use the purified N protein FIPV to protect more than 75% of tested animal from any FIPV infection. Applicants submit that while the N protein of type II FIPV has been shown to produce a protective immune response when it is delivered by a raccoon poxvirus, it fails to induce any protective immune response as evidenced by Vennema et al. (Virology 1991, Vol. 181, pp. 327-335, see Fig. 5). Another expertise, Susan Little also commented in 2010 that the theory using a cellular immune response to protect Feline Infectious Peritonitis infection has not been established in the art (Susan Little, Feline Infectious Peritonitis published on line in the website of WINIE FELINE FOUNDATION 2010, page 1-6). Wasmoen et al. also concluded that the unpredictability for using the N protein to induce a protective immune response may be related to 1). Differences in the physical properties of the expressed N proteins, 2). Differences of the replication abilities for carried expression vectors, 3). Altered magnitude or form of immune response to different expression vector, 4). Increased expression of the recombinant proteins by different expressing vector, and 5). Differences related to the rout of immunization and type of challenge models used (Adv. Exp. Med. Biol. 1995, Vol. 380, 221-228).

30. Regarding the issue for an adjuvant application for FIPV vaccine composition, the state of art teaches that different antigens are capable of inducing different immune response. Some of them are Th1 type and other is Th2 type. Some of them are capable of inducing humoral immune response, other may induce T cell response. There are also many types of adjuvants in the art as evidenced by Cox et al. (Chapter 4 ADJUVANS IN ADJUVANT TECHNOLOGY AND APPLICATION in Animal Parasite Control Utilizing Biotechnology Edited by W.K Yong, 1992,

pp. 49-112). Some of them are good for Th1 type and other is for Th2 type of immune response or both Th1 and Th2 type immune responses. In particular, Hebben et al. teach that different antigen proteins of FIPV can induce different (Th1 or Th2) immune responses. A reason for producing a better immune response by a modified vaccinia virus Ankara (MVA) strain as an expression vector for the FIPV M protein is that MVA-M can keep a better Th1/Th2 immune response balance (Journal of Feline Medicine and Surgery, 2004, Vol. 6, pp. 111-118).Therefore, selection of an appropriate adjuvant to boost the right type of immune responses is very important. Therefore, using an impropriate adjuvant may cause suppress the right immune response and potentiate a wrong immune response. For example, potentiating the humoral immune response of FIPV S antigen may cause more serious infection of the virus due to the ADE.

31. A broad scope of claims is directed to use any kind of adjuvants in combination. But the specification does not teach which mechanism is involved the protective immune response and which T cell epitope is responsible the protective T cell immune response. Specification also fails to provide a sufficient evidence to support the broad scope of claims encompassed astronomic number of species for the claimed N protein variants in combination with any adjuvant in the art.

32. Absence of all necessarily teaching and description discussed supra, A PhD level of immunology and virology is required to figure out 1). which immunological epitope is involved in T cell protective immune response, 2). what kind of Th1 or Th2 immune response is required for producing a protective immune response against FIPV infection; and 3). how to select an adjuvant to potentiate or balance the Th1 and/or Th2 immune response of the N protein antigen or its variants thereof in a vaccine composition.

33. As analysis above, it is concluded that an undue experimentation would be required to do fulfill the broad scope of claims encompassed with unexpected result.

Objection of Specification

34. The disclosure is objected to because of the following informalities: It is noted in page 42 section of adjuvant, the name of Felidovac PCR (Intervet) is different from the disclosure in the art as evidenced by STAR CAT RASKATTFORNING page 1-4 at web site http://stjankatten.se/art, search by 08/05/2010, in which the name of Felidovac PCR should be

Felidocav PRC. Please make an appropriate correction if the "PCR" should be spelled as "PRC". Appropriate correction is required.

35. Moreover, the use of the trademark Felidovac PRC has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. Appropriate correction is required.

36. Still further, it is noted that in page 42, the specification cites that a feline inactivated trivalent vaccine is used. But the specification does not describe which components are included in said trivalent vaccines. Please clarify which components are included in the trivalent feline vaccines in the adjuvant composition. An appropriate support for any amendment regarding to this clarification is required.

37.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BAO LI whose telephone number is (571)272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mondesi Robert can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bao Qun Li/

Examiner, Art Unit 1648